

Remarks

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Thus, claim 2 has been amended in response to items 3-5 under the rejection of the claims under the second paragraph of 35 U.S.C. §112. That is, amended claim 2 now clearly indicates where the list of labels ends; the expression "moiety with cell-inserting properties" has been deleted; and the "representing ..." language has been deleted (in both claims 2 and 17). Accordingly, the rejection based on items 3-5 has been rendered moot.

Applicants respectfully submit that these amendments should be entered even though they are presented after a final rejection, since the amendments clearly avoid some of the grounds of rejection without requiring any further consideration and/or search of the prior art.

The rejection of the claims under 35 U.S.C. §112 based on items 1-2 is respectfully traversed.

1. Methotrexate moiety

The skilled person in the art would easily recognize how methotrexate could be attached to a linker. He/she would indeed look at the oxygen and nitrogen functionalities in methotrexate in order to find the best way to attach methotrexate to a linker. The specification gives further guidance how to proceed. A substrate comprising a methotrexate label is exemplified in Examples 45 and 46, and shown in Scheme 15 (compound 78) and Scheme 16 (compound 79). However, methotrexate could also be attached by way of the other carboxyl function. The skilled person would also recognize that attachment could, in principle, be by one of the amino groups attached to the pterine nucleus.

2. Attachment of plurality of labels

The skilled person in the art, when reading in claim 2 that L is one or a plurality of the same or different labels connected to R₄, would immediately recognize that the linker must have two free valences for a single label, three for two labels, four for three labels, ... n+1 for n labels. Since the standard chemical language uses "alkyl" to indicate one free valence, "alkylene" to indicate two free valences, but has no standard expression for an alkane having three, four, ... n+1 free valences, the skilled person would conclude that "alkylene" should also be understood as a multivalent linker R₄.

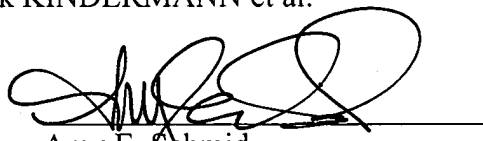
The specification gives further guidance about what is meant by a plurality of labels connected to R₄. Compound 54 in Scheme 9 (Example 25) and compounds 59 and 60 in Scheme 11 (Examples 30 and 31) are illustrative of two labels attached to a branched linker R₄.

Therefore, in view of the foregoing amendments and remarks, it is submitted that the rejection of the claims under 35 U.S.C. §112 has been overcome and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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